

Appendix B attached herewith.

**REMARKS**

Upon entry of the above amendment, claims 11-22 will be pending in the captioned application. Applicant respectfully submits that the amendments do not add any new matter within the meaning of 35 U.S.C. 132 to the application.

**1. Rejection of claims 15, 16, 21 and 22 under 35 U.S.C. §112,**

**1<sup>st</sup> paragraph**

The Official Action states the following, in relevant part:

Though applicants have limited the number of disorders considerably, replacing the extremely broad "airway disorder" with the list above, the number and types of conditions embraced by the language of claims 15, 16, 21 and 22 remains quite broad. Some of the conditions, like bronchitis, allergic bronchitis and rheumatoid arthritis, are distinct medical conditions, but others are nebulous, like COPD, arthritis and dermatitis. COPD...reads on conditions bearing no relation to the tryptase, such as emphysema caused by tobacco smoking, which is the result of corruption of alveolar tissue integrity. Dermatitis is caused by innumerable factors and "arthritis" embraces any inflammation of the joints, which is a common characteristic of many diseases.

**RESPONSE**

Applicant respectfully traverses this rejection.

However, solely in order to expedite the prosecution of this application, applicant has amended claims 15, 16, 21 and 22 to encompass even fewer diseases and disorders than previously claimed.

In particular, claims 15 and 21 have now been limited to the following six diseases and disorders: asthma, allergic conjunctivitis, allergic rhinitis, psoriasis, sclerodermatitis and inflammatory bowel disease. In order to demonstrate that tryptase inhibitors are enabled to treat these six diseases and disorders, applicants submit herewith an Information Disclosure Statement, citing two (2) references to Krishna, et al. and Rice, et al.

These two references demonstrate that it is well known by persons of ordinary skill in the art that tryptase inhibitors can be used in the treatment of asthma, allergic conjunctivitis, allergic rhinitis, psoriasis, sclerodermatitis and inflammatory bowel disease. Accordingly, a person of ordinary skill in the art would be enabled by the present specification to practice methods of treating such diseases and disorders by administering the tryptase inhibitors presently claimed.

**The Krishna, et al. reference**

The Examiner's attention is first drawn to the Krishna, et

al. reference entitled "Inhibition of mast cell tryptase by inhaled APC 366 attenuates allergen-induced late-phase airway obstruction in asthma", published in 2001. In this reference, Krishna, et al. discuss the use of a tryptase inhibitor in the treatment of asthma, allergic rhinitis, allergic conjunctivitis and sclerodermatitis.

In particular, applicant notes the data presented on page 1042 in Table I with regards to allergen challenges between APC 366 and placebo, and also in Table II with regards to the summary of data on physiological measurements and allergens used for bronchial challenges. Applicant further notes that in column 1 on page 1044, Krishna, et al. state that "[t]he present study demonstrates the potential role of APC 366 in the management of allergic disease, including asthma, allergic rhinitis and allergic conjunctivitis." Several lines later, Krishna, et al. state that "[t]hus, tryptase inhibitors might be useful for treating fibrotic diseases such as idiopathic pulmonary fibrosis and scleroderma, in which mast cell development has been noted."

Thus, Krishna, et al. have demonstrated that a person of ordinary skill in the art would be enabled by the present specification to practice methods of treating asthma, allergic

rhinitis, allergic conjunctivitis and sclerodermatitis by administering the tryptase inhibitors presently claimed.

**The Rice, et al. reference**

Reference is also made to the Rice, et al. reference entitled "Dibasic Inhibitors of human mast cell tryptase. Part 2: Structure-Activity Relationships and Requirements for Potent Activity", published in 2000. In this reference, Rice, et al. discuss the use of a tryptase inhibitor in the treatment of asthma, psoriasis and ulcerative colitis, i.e. inflammatory bowel disease.

In particular, applicant notes that Figure 1 on page 2365 demonstrates the effectiveness of the tryptase inhibitor APC-2059 in a sheep model of allergic asthma. Applicant further notes that in the abstract, Rice, et al. state that "APC-2059, a dibasic tryptase inhibitor with subnanomolar activity, has been advanced to phase II clinical trials for the treatment of both psoriasis and ulcerative colitis."

Thus, Rice, et al. have demonstrated that a person of ordinary skill in the art would be enabled by the present specification to practice methods of treating asthma, psoriasis and inflammatory bowel disease by administering the tryptase inhibitors presently claimed.

Accordingly, now that applicant has sufficiently demonstrated the enablement for the six diseases presently claimed, applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

**2. Rejection of claims 11-22 under 35 U.S.C. §112, 1<sup>st</sup> paragraph**

The Official Action states the following, in relevant part:

Claims 11-22 are rejected under 35 U.S.C. 112, 1<sup>st</sup> paragraph, because the specification, while being enabled for making salts, hydrates and salts of hydrates of the claimed compounds, does not reasonably provide enablement for making solvates in general of the claimed compounds.

Deletion of "a solvate" and "or a solvate of a salt thereof" in all occurrences would render the new rejection ... moot.

**RESPONSE**

Applicant respectfully traverses this rejection. However, solely to remove the basis for this rejection, applicant has deleted all occurrences of "solvate" and "or a solvate of a salt" from the claims. Thus, the basis for this rejection has been rendered moot.

Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

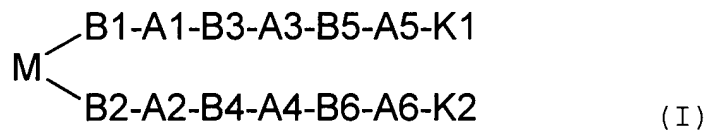
### 3. Objection to the Specification

The Official Action states the following in relevant part:

The abstract of the disclosure is objected to because structural variables M, B1, B2, B3, B4, B5, B6, A1, A2, A3, A4, A5, A6, K1 and K2 are referred to, along with the statement 'have the meanings indicated in the description', yet not [sic] structural formula of (I) is shown in the abstract.

A new abstract with the structural formula (I) is recommended. Correction is required.

Further to the Examiner's recommendation, applicant has submitted herewith an amended abstract of the disclosure containing the structural formula I:



Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

### 4. Allowable Subject Matter

The Official Action states that claims 11-14 and 17-20 would be allowable if rewritten or amended to overcome the rejections under 35 U.S.C. 112, 1<sup>st</sup> paragraph.

Applicant thanks the Examiner for this indication of

allowable subject matter and note that claims 11-22 have been amended in order to place all claims in condition for allowance.

**CONCLUSION**

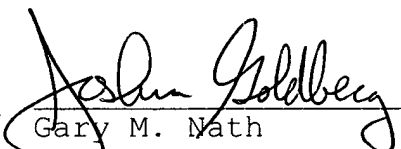
In view of the foregoing, applicant respectfully requests the Examiner to allow all claims pending in this application.

If the Examiner has any questions or wishes to discuss this matter, the Examiner is welcomed to telephone the undersigned attorney.

Respectfully submitted,

**NATH & ASSOCIATES PLLC**

Date: January 21, 2005  
**NATH & ASSOCIATES PLLC**  
1030 Fifteenth Street, N.W.  
Sixth Floor  
Washington, D.C. 20005-1503  
Telephone: (202) 775-8383  
Facsimile: (202) 775-8396  
JBG/SMM\ROA3.doc

  
\_\_\_\_\_  
Gary M. Nath  
Reg. No. 26,965  
Joshua B. Goldberg  
Reg. No. 44,126  
Sheldon M. McGee  
Reg. No. 50,454  
Customer No. 34375